Role of Tissue Doppler Imaging In Correlation With N-Terminal Pro-brain Natriuretic Peptide In Assessment Of Left Ventricular Diastolic Function In Egyptian Hypertensive Patient

Thesis

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List of contents

List of Tables

List of Figures

List of abbreviations

Abbreviation	Meaning
2HPP	2-hour plasma glucose
A	Maximum velocity of late mitral filling.
Aa wave	Late diastolic wave of the mitral annulus velocity by TDI
ACEI	Angiotensin Converting Enzyme Inhibitor.
ACS	Acute Coronary Syndrome
AGEs	Advanced Glycation End products
Am	Peak late diastolic velocity in the myocardium
ANP	Atrial Natriuretic Peptide
BMI	Body Mass Index.
BP	Blood pressure
CHARM study	Candesartan in Heart failure – Assessment of Reduction in Mortality and morbidity study in Preserved EF
CHD	Coronary heart disease
CHF	Congestive heart failure
CNP	C-type Natriuretic Peptide
Colour-TDI	Colour Tissue Doppler Imaging.
CRP	C-reactive protein
CT	Computed tomography
CVD	Cardio-Vascular Diseases
DBP	Diastolic blood pressure.
DHF	Diastolic Heart Failure
DM	Diabetes Mellitus.
DNP	Dendroaspis Natriuretic Peptide
DT	Deceleration Time
E	Maximum velocity of early mitral filling
Ea wave	Early diastolic wave by the mitral annulus velocity by TDI
ECG	Electrocardiogram
EDPVR	End-Diastolic Pressure-Volume Relationship
EF	Ejection Fraction
Em	Peak early diastolic velocity in the myocardium
FS	Fractional Shortening.
HF	Heart Failure
HFNEF	Heart failure with Normal Ejection Fraction
HFPEF	Heart failure with Preserved Ejection Fraction
HHD	Hypertensive Heart Disease.
LA	Left atrium
LV	Left Ventricle

LVEDD	Left ventricular end diastolic diameter
LVEDP	Left ventricular end diastolic pressure
LVEF	Left Ventricular Ejection Fraction.
LVESD	Left ventricular end systolic diameter
LVH	Left Ventricular Hypertrophy
LVM	Left ventricular mass.
MI	Myocardial Infarction
MMP	Matrix Metalloproteinases
MRI	Magnetic resonance imaging
NO	Nitric Oxide
NTPBNP	N Terminal Pro Brain Natriuretic Peptide
NYHA	New York Heart Association
PCWPm	mean Pulmonary Capillary Wedge Pressure
PE	Pulmonary Edema
PLB	Phospholamban
PNF	Pseudonormal filling
PWT	Posterior wall thickness
PW-TDI	Pulsed-Wave Tissue Doppler Imaging.
RAAS	Rennin Angiotensin Aldosterone system.
ROI	Region of interest
RWT	Relative wall thickness
Sa	Peak systolic velocity at the mitral annulus by TDI
SBP	Systolic blood pressure
SD	Standard deviation
SERCA	Ca2+ adenosine triphosphatase of the SR
Sm	Peak systolic velocity in the myocardium by TDI
SR	Sarcoplasmic Reticulum
TDE	Tissue-Doppler Echocardiography.
TDI	Tissue Doppler Imaging
TGF1	Transforming Growth factor 1
TIA	Transient ischemic attack
TOD	Target organ damage
TTE	Transthoracic echocardiography
TVI	Tissue velocity imaging
U.S.	United States
Vp	Flow propagation velocity
VST	Ventricular septal thickness
WHO	The World Health Organization

Abstract

Tissue Doppler imaging of the mitral annulus may predict the diastolic filling of left ventricle. **Objectives:** we investigated the pattern of diastolic function in a subset of hypertensive patients and evaluated the correlation between mitral annular TDI velocities & plasma level of NT pro BNP and its predictive cutoff value to diagnose LV diastolic dysfunction. **Methods**: After full clinical examination, we prospectively measured plasma level of NT pro BNP, assessed LVH by both ECG, Echo. we measured LV EF, Left atrial diameter , left venricular geometry and assessed LV diastolic function by both mitral flow pattern & mitral annular TDI parameters, in 40 Asymptomatic patients with normal EF (more than 55%) and 20 healthy control subjects. **Results:** We found that Ea velocities were decreased in hypertensive group with diastolic dysfunction. Moreover, E/Ea ratio was higher in hypertensive group(p=0.04) .the E/Ea was significantly& directly correlated with the level of NT pro BNP(r=0.41,P=0.008). The powerful predictors of NT pro BNP level in hypertensive patients with diastolic dysfunction were E/Ea(r=0.41,P=0.008), LVMI(r=0.41,P=0.015) and duration of hypertension(r=0.6,P=0.0001). Moreover, the powerful predictor of concentric LVH geometry is the duration of the hypertension(r=0.42, P=0.01). The cutoff point of NT pro BNP plasma level to detect diastolic dysfunction in asymptomatic hypertensive patient were 40.7 pg/ dl (sensitivity 95% and specificity 84%). **Conclusion:** Combination of tissue Doppler parameter and NT pro BNP plasma level offers a new strategy of risk stratification in hypertension. NT pro BNP is a promising marker to detect the subclinical state of heart failure with normal ejection fraction especially in hypertensive patient with diastolic dysfunction.

Key words: Systemic hypertension, Diastolic dysfunction, NT pro BNP, Tissue Doppler imaging, LV geometry.

Introduction

Hypertension is a major health problem in Egypt with a prevalence rate of 26.3% among the adult population (> 25 years). Its prevalence increases with aging, approximately 50% of Egyptians above the age of 60 years suffer from hypertension **(Ibrahim MM, et al., 1995).**

Risks of hypertension include cardiovascular complications (heart failure, myocardial infarction, atrial fibrillation, aneurysms, dissection), renal (azotemia) and cerebrovascular (stroke, transient ischemic attacks "TIA", dementia), resulting in disability and premature death. These risks can be reversed by treatment and control of hypertension.

Hypertension is poorly managed in Egyptians. The rates of awareness, treatment and control are low. Only 8% of hypertensive Egyptians have their blood pressure controlled **(Ibrahim MM, et al., 1995).**

A new paradigm is emerging related to the impact of chronic hypertension on the cardiac parenchyma. In fact , although macroscopic left ventricular hypertrophy (LVH)is the hallmark of hypertensive heart disease(HHD), a number of changes in the cardiomyocyte components of the myocardium also develop in hypertension that alter the composition and structure of the myocardium.The occurrence of these alterations may explain why the presence of LVH is independently associated with increased risk of cardiac complication namely heart failure in hypertensive patients. Whereas LVH may be detected early and accurately in hypertensive patients by electrocardiography (ECG) and Echocardiography, newer cardiac imaging , and monitoring of several circulating biomarkers hold promise as noninvasive tools for the diagnosis of myocardial remodeling **(Diez J, et al.,2009).** .

Extending the utility of BNP as a diagnostic marker to screen for asymptomatic or preclinical ventricular dysfunction (Stage B heart failure) according to the ACC/AHA guidelines in the general population has not proved cost-effective as the prevalence of heart failure is low **(Hunt SA, *et al.,2005).***

However, if the test is used in patients stratified for risk using clinical criteria, BNP has proved useful to "rule out" ventricular dysfunction, thus eliminating the need for other more expensive diagnostic tests in this group **(Yamamoto K, et al.,2000).**

Of all investigated neurohormones and natriuretic peptides, B type natriuretic peptide and N-terminal pro BNP are the best markers for ruling out left ventricular dysfunction and to detect the degree of severity. Although the current value of amino-terminal pro–B-type natriuretic peptides (NTproBNP) to generally screen populations of "apparently well patients" remains promising but still undefined, its role in the evaluation of patients with essential hypertension (EHT) is less clear. The use of NT-proBNP to screen patients at high risk for heart disease (such as elderly patients, or patients with diabetes mellitus, hypertension,or known coronary artery disease) appears logical and is supported by data **(Hammerer A, et al., 2004).**

NT-proBNP has strong prognostic value in such at-risk patients. However, the exact implications for clinical management after detection of an elevated NT-proBNP value should be driven by clinical judgment. At present, data suggest that when an elevated NT-proBNP is detected in an at-risk patient, it is a high-risk finding **(Vincent E, et al., 2008).**

LVH is a common finding in patients with fixed or borderline hypertension and can be diagnosed either by ECG or by echocardiography. Echocardiography is the procedure of choice, since the sensitivity of the different ECG criteria may be as low as 7 to 35 percent with mild LVH and only 10 to 50 percent with moderate to severe disease **(Marwick TH, et al., 2007**).

Echocardiography is an excellent noninvasive tool for the assessment of ventricular size and both systolic and diastolic function, and it is routinely used in patients with heart failure. The evaluation of diastolic function is not easily obtained by other techniques, and this feature is where echocardiography has its advantages. **(Marwick TH, et al., 2007**).

In practice, a normal ejection fraction (EF) on 2-D echocardiography in patients with clinical evidence of heart failure immediately suggests the potential diagnosis of left ventricular (LV) diastolic dysfunction. Doppler, color flow imaging, and myocardial tissue imaging can confirm or exclude the diagnosis of LV diastolic dysfunction by assessing valvular abnormality and intrinsic diastolic function and estimating diastolic filling pressure **(Oh JK, et al., 2005)**.

Several findings suggest that the peak velocity of early diastolic displacement of the annulus is a relatively preload independent index of global LV function that can be useful in unmasking pseudo normalization of the mitral inflow **(Ommen SR, et al., 2000).**

Because of its high reproducibility, feasibility, and relatively preload-independence, tissue Doppler recording of the early diastolic mitral annular velocity (Ea) in conjunction with the mitral inflow velocity (E) has become the first line of diastolic evaluation. Myocardial relaxation is impaired in almost all patients with diastolic dysfunction, which is best assessed by the Ea velocity of the mitral annulus using TDI. While early diastolic trans-mitral velocity (E) increases progressively as LV filling pressure increases, the mitral annular Ea velocity remains decreased at all stages of diastolic dysfunction **(Marwick TH, et al., 2007).**

Early identification of diastolic dysfunction in asymptomatic (stage B) patients by echocardiography may provide an opportunity to manage the underlying etiology appropriately to prevent its progression to overt DHF (stage C of development of heart failure) (**Marwick TH, et al., 2007)**.

Aim of work

- To assess left ventricular diastolic function in Egyptian hypertensive patient by Pulsed Wave Tissue Doppler imaging (PW-TDI).

- To identify the predictive value of NT- pro BNP in the diagnosis of left ventricular diastolic dysfunction in Egyptian hypertensive patient.

- To find the correlation between LV diastolic function & NT pro BNP level.